NATIONAL MARROW DONOR PROGRAM®

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GRANT AWARD N00014-05-1-0310
QUARTERLY
PERFORMANCE / TECHNICAL REPORT
For the Period
JANUARY 1, 2007 to MARCH 31, 2007

GRANT AWARD N00014-05-1-0859
QUARTERLY
PERFORMANCE / TECHNICAL REPORT
For the Period
JANUARY 1, 2007 to MARCH 31, 2007

AND

GRANT AWARD N00014-06-1-0704
QUARTERLY
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For the Period
JANUARY 1, 2007 to MARCH 31, 2007

Office of Naval Research

And

The National Marrow Donor Program
3001 Broadway Street N.E.
Minneapolis, MN 55413
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REPORT DOCUMENTATION PAGE

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13. SUPPLEMENTARY NOTES
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14. ABSTRACT
Task 1 : Evaluate optimal short term storage parameters for stimulated and unstimulated leukapheresis (donor lymphocytes) and bone marrow products, including the type of storage media and the cell concentration, in addition to temperature and duration of storage before processing or infusion.

Task 2: The NMDP has developed an algorithm that "predicts' high resolution HLA typing results on donor samples that exist in the Registry with only low or intermediate results reported. Perform validation of the NMDP algorithm by selecting donors randomly from our Registry that have low or intermediate DRB1 typing results and using the algorithm to predict the high resolution results and test the ability of the algorithm to predict KIR ligand mismatching in the absence of existing HLA-C locus results.

15. SUBJECT TERMS
Research in HLA Typing, Hematopoietic Stem Cell Transplantation and Clinical Studies to Improve Outcomes

16. SECURITY CLASSIFICATION OF:			17. LIMITATION OF ABSTRACT	18. NUMBER OF PAGES	19a. NAME OF RESPONSIBLE PERSON
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National Marrow Donor Program® N00014-05-1-0310
HLA Typing for Bone Marrow Transplantation
Progress Report for the Period 9 Funding
January 1, 2007 – March 31, 2007

Task 1: Product Validation

Description:

The objective of this study is to evaluate optimal short term storage parameters for stimulated and unstimulated leukapheresis (donor lymphocytes) and bone marrow products, including the type of storage media and the cell concentration, in addition to temperature and duration of storage before processing or infusion.

Project 1. Effects of Media Storage and Cell Concentration

Stimulated and unstimulated leukapheresis and bone marrow products that are representative of products collected and provided for NMDP transplant patients will be purchased. Aliquots of the product will be stored in different storage media at varying cell concentrations per mL of media. Standard graft characterization parameters will be tested.

Objectives:

1. Transportation factors: Determine the effects of different types of tissue media, nucleated cell concentration on CD34+ cell, CD3+ and total nucleated cell viability, and CFU-GM frequency during transport from collection sites to the transplant centers.
2. Overnight storage factors: Determine the effects of different type of tissue media, type of storage bags (gas permeable or non gas permeable), nucleated cell concentration on CD34+, CD3+ cell and total nucleated cell viability, and CFU-GM frequency during overnight storage.

Project 2. Effects of Time and Temperature

Stimulated and unstimulated leukapheresis and bone marrow products that are representative of products collected and provided for NMDP transplant patients will be purchased. Aliquots of the product will be stored at varying lengths of time and temperature. Standard graft characterization parameters will be tested.

Objectives:

1. Temperature factors: Determine the optimal short term storage temperature to preserve nucleated cell count, percent viable TNC, CD34+ and CD3+ cells, CFU-GM frequency and sterility.
2. Time factors: Determine the effect of time on nucleated cell count, percent viable TNC, CD34+ and CD3+ cells, CFU-GM frequency and sterility.

Activity:

The original period of performance for the Product Validation Study was set to be complete February 2, 2007. Due to delays encountered by the laboratory, a six month extension was applied for and granted. The period of performance was extended until August 2, 2007. Sample testing was completed this quarter and consisted of one unstimulated PBMC, two mobilized PBSC and five marrow samples. Analysis of all study data began during the quarter and will be completed and reported to the NMDP early in the next quarter.

National Marrow Donor Program® N00014-05-1-0310
HLA Typing for Bone Marrow Transplantation
Progress Report for the Period 9 Funding
January 1, 2007 – March 31, 2007

Task 2: Validation of the Expectation – Maximization (EM) Algorithm

Description:

The NMDP has developed an algorithm that "predicts' high resolution HLA typing results on donor samples that exist in the Registry with only low or intermediate results reported. A modified version of this algorithm predicts HLA results at loci where there are no typings based on existing typings at other loci and the ethnic-specific haplotype frequencies observed in the population.

It is our intention to incorporate this logic into the mechanisms used to select matched donors for patient searches. Incorporation of this logic would improve the specificity of donors that appear on patient's searches, which then decreases the costs and time necessary to identify the optimally matched donor. This logic will also be used to provide estimates of the likelihood of finding matched donors in the Registry including matching at loci where some donors in the Registry do not currently have typings.

A portion of the funding would be used to assist in the validation of the NMDP algorithm by selecting donors randomly from our Registry who have low or intermediate DRB1 typing results and using the algorithm to predict the high resolution results. The HLA typing results would be used to validate the accuracy of this method in an unbiased data set.

The remaining portion of the funding would be used to test the ability of the algorithm to predict KIR ligand mismatching in the absence of existing HLA-C locus results. Randomly selected donors from the Registry without HLA-C would be run through a modified version of the algorithm to predict the C locus KIR ligand status. The HLA intermediate resolution typing would validate the accuracy of this method in an unbiased data set.

A laboratory would perform the high resolution HLA-DRB1 testing and/or intermediate resolution HLA-B and C from stored samples of the donors. Quality control and performance criteria will be monitored by a Scientific Services Specialist. The results will be analyzed by a programmer in the Bioinformatics group to verify the accuracy of each prediction technique.

In addition to assisting with the validation of the algorithm, this typing project has potential to impact subsequent patient searches simply due to the increased level of resolution for the Registry donors whose typings have been upgraded. A portion of this typing may be selected on behalf of searching patients in order to further validate the approach and provide direct positive impact on these searches.

Activity:

This Task was completed in a previous period.

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National Coordinating Center
3001 Broadway St. N.E.
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April 27, 2007

Commander Russell Shilling, USN
Program Officer, Medical Services Corps
Office of Naval Research (ONR 341)
875 N. Randolph St.
Arlington, VA 22203

Subject: Quarterly Performance/Technical Report of the National Marrow Donor Program®

Reference: Grant Award #N00014-05-1-0859 between the Office of Naval Research and the National Marrow Donor Program

Dear Commander Shilling:

Enclosed is subject document which provides the performance activity for each statement of work task item of the above reference for the period of January 1, 2007 to March 31, 2007.

Should you have any questions as to the scientific content of the tasks and the performance activity of this progress report, you may contact our Chief Operating Officer - Patricia Coppo directly at 612-627-5815.

With this submittal of the quarterly progress report, the National Marrow Donor Program has satisfied the reporting requirements of the above reference for quarterly documentation. Other such quarterly documentation has been previously submitted under separate cover.

Please direct any questions pertaining to the cooperative agreement to my attention (612-362-3403 or at cabler@nmdp.org).

Sincerely,

Carla Abler-Erickson

Carla Abler-Erickson, MA
Sr. Contracts Representative

Enclosure: One (1) copy of SF298
One (1) copy of subject document

c: R. Baerga – ACO (ONR-Chicago), letter and enclosure
Dr. Robert J. Hartzman, CAPT, MC, USN (Ret): letter and enclosures
DTIC (Ste 0944): letter and enclosures
NRL (Code 5227): letter and enclosures
Brian Bradley – Grants Officer (ONR-252), letter and enclosure
Patricia A. Coppo, Chief Operating Officer, NMDP, letter only

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14. ABSTRACT

1. Contingency Prepardness: Collect information from transplant centers, build awareness of the Transplant Center Contingency Planning Committee and educate the transplant community about the critical importance of establishing a nationwide contingency response plan.

2. Rapid Identification of Matched Donors : Increase operational efficiencies that accelerate the search process and increase patient access are key to preparedness in a contingency event.

3. Immunogenetic Studies: Increase understanding of the immunologic factors important in HSC transplantation.

4. Clinical Research in Transplantation: Create a platform that facilitates multicenter collaboration and data management.

15. SUBJECT TERMS
Research in HLA Typing, Hematopoietic Stem Cell Transplantation and Clinical Studies to Improve Outcomes

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QUARTER PROGRESS REPORT

Development of Medical Technology for Contingency Response to Marrow Toxic Agents

January 1, 2007 through March 31, 2007

TABLE OF CONTENTS

ACRONYM LIST

AABB – American Association of Blood Banks
AML – Acute Myelogenous Leukemia
ARS – Acute Radiation Syndrome (also known as Acute Radiation Sickness)
ASBMT – American Society for Blood and Marrow Transplantation
ASHI – American Society for Histocompatability and Immunogenetics
B-LCLs – B-Lymphoblastoid Cell Lines
BMT-CTN – Blood and Marrow Transplant - Clinical Trials Network
C&A – Certification and Accreditation
CBMTG – Canadian Blood and Marrow Transplant Group
CBB – Cord Blood Bank
CBC – Congressional Black Caucus
CBS – Canadian Blood Service
CBU – Cord Blood Unit
CHTC – Certified Hematopoeitic Transplant Coordinator
CIBMTR – Center for International Blood & Marrow Transplant Research
CLIA – Clinical Laboratory Improvement Amendment
CME – Continuing Medical Education
CRCS – Critical Staff Recovery Site
CREG – Cross Reactive Groups
CSS – Center Support Services
CT – Confirmatory Typing
CTA – Clinical Trial Application
DIY – Do it yourself
DKMS – Deutsche Knochenmarkspenderdatei
DMSO - Dimethylsulphoxide
DNA – Deoxyribonucleic Acid
D/R – Donor/Recipient
EBMT – European Group for Blood and Marrow Transplantation

EM – Expectation Maximization
EMDIS – European Marrow Donor Information System
FBI – Federal Bureau of Investigation
FDA – Food and Drug Administration
FMHQ – Family Medical History Questionnaire
Fst – Fixation Index
GETS – Government Emergency Telecommunications Service
GCSF – Granulocyte-Colony Stimulating Factor (also known as filgrastim)
GI – Gastro Intestinal
GVHD – Graft vs Host Disease
HHS – Health and Human Services
HIPAA – Health Insurance Portability and Accountability Act
HLA – Human leukocyte antigen
HMD – Histoimmunogenetics Mark-up Language
HML – *Histoimmunogenetics* Mark-up Language
HR – High Resolution
HRSA – Health Resources and Services Administration
HSC – Hematopoietic stem cell
IBWC – Immunobiology Working Committee
IDM – Infectious disease markers
IHWG – International Histocompatibility Working Group
IND – Investigational New Drug
ICRHER – International Consortium for Research on Health Effects of Radiation
IS – Information services
IT – Information technology
IRB – Institutional Review Board
IHWG – International Histocompatibility Working Group
KIR – Killer Immunoglobulin-like Receptor
NCI – National Cancer Institute
MHC – Major Histocompatibility Complex
MICA – MHC Class I-Like Molecule, Chain A

MICB – MHC Class I-Like Molecule, Chain B
MRQ – Maternal Risk Questionnaire
MUD – Matched Unrelated Donor
NCBM – National Conference of Black Mayors
NCI – National Cancer Institute
NHLBI – National Heart, Lung and Blood Institute
NIAID – National Institute for Allergy and Infectious Disease
NIH – National Institutes of Health
NIMS – National Incident Management System
NK – Natural Killers
NMDP – National Marrow Donor Program
NRP – National Response Plan
NST – Non-myeloablative Allogeneic Stem Cell Transplantation
OCR/ICR – Optical Character Recognition/Intelligent Character Recognition
OIT – Office of Information Technology
OMB – Office of Management and Budget
ONR – Office of Naval Research
PBMCs – Peripheral Blood Mononuclear Cells
PBSC – Peripheral Blood Stem Cell
PCR – Polymerase Chain Reaction
P-LCLs – B-lymphoblastoid cell lines
PSA – Public Service Announcement
QC – Quality control
RCC – Renal Cell Carcinoma
REAC/TS – Radiation Emergency Assistance Center/Training Site
RFP – Request for Proposal
RFQ – Request for Quotation
RITN – Radiation Injury Transplant Network
SBT – Sequence Based Testing
SCTOD – Stem Cell Therapeutics Outcome Database
SG – Sample Group

SSP – Sequence Based Priming
SSOP – Sequence Specific Oligonucleotide Probes
STAR® – Search, Tracking and Registry
TC – Transplant Center
TED – Transplant Essential Data
TNC – Total Nucleated Cell
TSA – Transportation Security Agency
URD – Unrelated Donor
WMDA – World Marrow Donor Association
WU – Work-up

II.A. Contingency Preparedness – Hypothesis 1: Recovery of casualties with significant myelosuppression following radiation or chemical exposure is optimal when care plans are designed and implemented by transplant physicians	

Aim A.1.1: Secure Interest of Transplant Physicians	**Period 6 Activity:**
	
	<u>Funding provided by both 0859 and 0704 contracts this quarter:</u>
	• Initiated planning of physician radiological/nuclear emergency training seminar:
	  o Scheduled for September 25, 2007 in Bethesda, MD.
	  o Seminar title: Medical and organizational challenges resulting from a radiological or nuclear emergency.
	  o Anticipating 150 attendees.
	  o Seminar objective: Inform attendees of the biological risk factors and medical complications resulting from ionizing radiation exposure and to diagnose various resulting injuries.
	  o Program description: Presentations of the impact to the US and the medical challenges that would arise due to an ionizing radiation event
	  o Learning objectives:
	  ▪ Understand the current radiation/nuclear threat to the US.
	  ▪ Describe biological effects of ionizing radiation on the multiple organs (skin, hematological, GI, neurological, and multi-organ failure).
	  ▪ Explain basics of calculating radiation dose based on bio-dosimetry.
	  ▪ Describe current concept of operations from triage through delivery of care or transfer to another treatment facility.
	  ▪ Hospital management of severely injured radiation patients.
	• Began the development of a standardized RITN ARS Grand Rounds presentation for use by all RITN centers.

Aim A.1.2: GCSF in Radiation Exposure	**Period 6 Activity:** • No activity this period.

Aim A.1.3: Patient Assessment Guidelines	**Period 6 Activity:** Incorporating transplant treatment options in RITN ARS Grand Rounds presentation development. NMDP Information Technology (IT) department continues to upgrade and enhance the NMDP information and communication structures. Cord bank data conversion to CORD Link continue: • CBB 180 Colorado was converted and over 5000 cords were made available. • CBB 158 Texas made >400 cords AV. • CBB 193, Sheba data file was received. • CBB 192, Singapore – files have been received. Waiting for additional data. • Gift of Life has completed their coding for inventory transactions for cord. Testing will begin soon. Enhanced CORD Link Web to support requested services from cord blood banks. Features were added to support New FDA Guidance for IDM NAT HIV/HCV. On January 24, 2007, the FDA issued guidance mandating Maternal IDM NAT HIV/HCV Testing to be performed using individual testing methods per manufacturer's requirements instead of pooled testing. This impacts CBUs collected on or after May 25, 2005. CBU inventory that was tested using the pooled method must be retested prior to release for transplantation. Each NMDP CBB has identified their affected inventory. On February 22, the affected inventory began being labeled with a new Report Card Status: "PreOrder Condition". This is the indicator that additional testing is required before the CBU can be shipped for transplant. Features were added to support Local IDs and ISBT ID Fields. This has allowed the CBBs to enter their entire Local CBU ID and Local Maternal ID or ISBT ID into the CORD Link application, without truncation. NMDP continues to enhance the SEARCH Link™ and TRANS Link® applications. To comply with the January 24, 2007, FDA issued guidance as indicated above, a new Qualification Status "Pre-Order Condition" was added which indicates additional testing is required by the CBB prior to transplantation. CBU Inventory where a pooled testing method was utilized for NAT HIV/HCV testing will all be labeled with the Pre-Order Condition, until results are entered by the CBB. To improve operational efficiencies and decision making for the Transplant Center and the Search and Transplant Services department reorganization of the display of information on cord processing, viability, CBU

	testing was made. Also, reorganization of several reports within the applications was made. To comply with the US Energy Policy Act of 2005 (EPACT) mandate that Daylight Saving Time (DST) in the United States of America start on the second Sunday in March and end on the first Sunday in November starting in 2007, necessary patches on systems and applications were required and installation completed. Development for the TRANS Link Web project is underway. The focus is upon improving reliability and availability of the application, while incorporating changes to the NMDP business process. These two goals will help to improve the customer experience. Additionally, we will reduce the number of applications that our customers require to do business with NMDP. Work to date has focused on implementing features that can leverage the ongoing work of the Unification Data Model (UDM) project. TRANS Link will reap benefits of the new consolidated data model as they become available. This will allow TRANS Link Web to more easily integrate NMDP search results with those of cooperative registries or BMDW. The Research Repository software was enhanced to add the ability to send samples from the Research Repository to a contract tissue culture lab for cell transformation and expansion. The feature required repurposing the shipment architecture. In addition, enhancements were made to support the consolidation of the inventory and creation and population of a master repository. As an operational efficiency, IT enhanced the repository software, CRIS Link, and added features to allow for multiple buccal swabs to be shipped for High Resolution (HR) requests.
Aim A.1.4: National Data Collection Model	**Period 6 Activity:** • No activity this period.

IIA Contingency Preparedness – Hypothesis 2: Coordination of the care of casualties who will require hematopoietic support will be essential in a contingency situation.

Aim A.2.1: Contingency Response Network	**Period 6 Activity:** **Funding provided by both 0859 and 0704 contracts this quarter:** **Planning:** • Developed a RITN Web site outside the NMDP Network site (www.nmdp.org/ritn) • Created and distributed RITN SOP templates for TCs, DCs, and CBBs. • Coordinated approval for release of sanitized TC SOP as an example for other RITN centers. • Produced and distributed a contact list with RITN points of contact, key federal agencies and state emergency operation center contacts. • Created organization level Emergency Response Plan, and coordinated training of all staff during 3rd quarter. **Exercises:** • Participated in a regional tabletop exercise held by the MN Federal Executive Board, focusing on the detonation of an Improvised Nuclear Device (IND). **Meetings:** • Presented a RITN overview presentation to HHS-NCI parallel preparedness initiative. • Held a RITN meeting at the ASBMT/CIBMTR Tandem Meetings in February. • Continued to coordinate signing of RITN agreements; as of April 11, 2007, 73% (44 of 60) of invited centers have signed participation agreements. • Attended the NIAID Radiation Combined Injury Workshop in Bethesda, MD. • Assisted multiple RITN centers in developing their response plans (support provided via conference call). • Performed a site visit at Barnes Jewish to consult on their development of RITN SOPs. **Communications:** • Purchased and distributed additional satellite telephones; a total of 36 phones are distributed to RITN centers. • Distributed additional GETS cards; there are a total of 114 cards between NMDP staff and RITN centers.

	• Conducted communication tests with the Network (January and March) and a GETS card user test.
Aim A.2.2: Sibling Typing Standard Operating Procedures	**Period 6 Activity:** • Established project priority for FY2008, to develop manual procedures for processing sibling typing.
II.A. Contingency Preparedness – Hypothesis 3: NMDP's critical information technology infrastructure must remain operational during contingency situations that directly affect the Coordinating Center.	
Aim A.3.1: I.S. Disaster Recovery / Business Continuity Planning	**Period 6 Activity:** • Business Continuity Planning: o Identified 8 options for Critical Staff Recovery Site (CSRS). o Further developed cost benefit analysis of CSRS. o Presented CSRS options to Chief Financial Officer and Chief Medial Officer. o Conducted hazard assessment and created a mitigation plan for the New Brighton Repository facility. o As part of the Business Continuity Plan re-write: initiated Business Impact Analysis of all critical functions conducted at the MPLS Coordinating Center. Performed the 17th Disaster Recovery Test in January 2007. This utilized the servers and replicated databases which are in place at the data recovery site in Leawood, Kansas. The majority of the recovery work was performed remotely from the NMDP Repository site in New Brighton, MN. This was the first test to take advantage of real time data replication of critical databases. As a result the recovery efforts were completed 33% faster than the previous tests.
II.B. Rapid Identification of Matched Donors – Hypothesis 1: Increasing the resolution and quality of the HLA testing of volunteers on the registry will speed donor selection.	
Aim B.1.1: Increase Registry Diversity	**Period 6 Activity:** STAR Link Web was enhanced to support increased donor recruitment. "Do It Yourself" Donor (DIY) registration through www.marrow.org completed in the previous quarter resulted in the registration of 4500 with

	another 1500 in process. Functionality to support use of DIY "Promotion Codes" or "Coupons" for sponsored payment of recruitment costs was added. Code has been completed and is in test on the "Forward to a friend" project which will allow email forwarding and tracking of promotion codes to other emails. The prototype has been completed on the "DIY Dashboard" for recruitment metrics and analysis. Enhancements were made to for phase 1 of the drive redesign. This feature allows for entry of drive estimates to be entered into STAR Link Web. This feature will eventually allow donor centers to automatically setup drives by managing their estimates against goals in the FDR business application. Features were also added to enhance the ability to order sample kits that are sent to the donors for recruitment typing and donor centers for search typing. The Kit Maker application was also enhanced to prioritize kits for expedited patient drives. This will allow for guaranteed same date shipment and storage when the kits are returned. **Registry HLA-A,B,DR typing** • Completed testing of 43,184 newly recruited volunteer donors • Blind quality control testing error rate was 0.04%, satisfying the project requirement of 1.5% Testing turnaround time was 98% for Class I and II combined, meeting the project requirement of 85% of typing results reported within 14 days from shipment of samples.
Aim B.1.2: Evaluate HLA-DRB1 High Res typing	**Period 6 Activity:** • This task is closed.
Aim B.1.3: Evaluate HLA-C Typing of Donors	**Period 6 Activity:** • A preliminary report was prepared and discussed with the DNA Project Officer. Further analysis was requested and will be completed by September 2007. **Impact of HLA-C typing on HR/CT/WU rates** • Primary analysis included 20,182 donors from the DoD Donor Center with & without C typing over the

course of the study period

- Because all donor registration did not occur simultaneously, a statistical method based on exposure times and person-year events was used
- Secondary analysis eliminated bias by restricting to donors with C at the time of recruitment (n=5906)
- The impact of race was analyzed in the subgroup
- The timeframe was March 2003 – September 2006

	Group	HR	CT	WU
Number of	No C	213	507	26
Events	With C	12	137	12
Person-years	No C	45359	45519	939
Exposure on Reg	With C	3199	3209	259
Event rate per	No C	.0047	.011	.028
Person-year	With C	.0038	.043	.046
P-value		0.549	<0.001	0.201

Analysis summary:

- Donors with C typing available go to CT more often than donors without (this was statistically significant)
- Donors without C typing go to HR at a higher rate (this was not statistically significant)
- There was no statistical significance shown for WU rates, although there was a trend for higher WU rates from donors that had C
- Results may be impacted by loss of statistical power in the small endpoint groups (12 donors)

	• We were not able to demonstrate impact on search time • More data and/or longer time frame needed
Aim B.1.4: Evaluate Buccal Swabs	**Period 6 Activity:** **Alternative cell type for blind Quality Control Swab Samples** • Evaluation and optimization of alternative cell types for QC swab samples was completed. • B-LCL cell lines from the NMDP Research Sample Repository and high resolution HLA typed through the Donor/Recipient Pair project were selected as the optimal alternative cell type. All 5 contract labs and the Navy lab were able to accurately and successfully type all swabs created with B-LCL cells. • 25 cell lines are being expanded at a contract lab to provide cells for QC swab creation. • A designated laboratory space is being set up at the Repository for generation of QC swabs. Materials needed to create B-LCL QC swabs were ordered including; a bench top centrifuge, vortex, magnetic stir plate, pipettes and reagents and consumables for washing and resuspending the cells. As soon as all equipment is received, protocols will be tested and initial swabs will be sent to all labs for final evaluation. • An additional 900 buccal swabs have been collected from current QC donors within the NMDP to supply the three contract labs requiring real buccal cells for QC testing. The other two contract labs are still receiving purified DNA dipped QC swabs.
II.B. Rapid Identification of Matched Donors – Hypothesis 2: Primary DNA typing data can be used within the registry to improve the quality and resolution of volunteer donor HLA assignments.	
Aim B.2.1: Collection of Primary Data	**Period 6 Activity:** • No activity this period.
Aim B.2.2: Validation of Logic of Primary Data	**Period 6 Activity:** • No activity this period.

Aim B.2.3: Reinterpretation of Primary Data	**Period 6 Activity:** • No activity this period.
Aim B.2.4: Genotype Lists & Matching Algorithm	**Period 6 Activity:** • No activity this period.
II.B. Rapid Identification of Matched Donors – Hypothesis 3: Registry data on HLA allele and haplotype frequencies and on the nuances of HLA typing can be used to design computer algorithms to predict the best matched donor.	
Aim B.3.1: Phase I of EM Haplotype Logic	**Period 6 Activity:** • Scientific Services and Bioinformatics staff summarized the data generated from the review of the EM algorithm validation. This included the review of all the items tracked in the NMDP ClearQuest system that were generated by the validation so that we could capture the resolution of all outstanding issues.
Aim B.3.2: Enhancement of EM Algorithm	**Period 6 Activity:** • Project meetings were held to plan the database modeling, design and development for Haplogic II.
Aim B.3.3: Optimal Registry Size Analysis	**Period 6 Activity:** • No activity this period.
Aim B.3.4: Target Under-represented Phenotypes	**Period 6 Activity:** • No activity this period.
Aim B.3.5: Bioinformatics Web Site	**Period 6 Activity:** • No activity this period.

Aim B.3.6: Maximize software using consultant data	**Period 6 Activity:** • All NMDP HLA search strategy advisors completed 381 search reviews for 88 transplant centers in this quarter. External advisors completed 241 reviews with an average turnaround time of 4.4 business days; internal advisors provided 140 reviews with an average turnaround time of 2.6 business days. The average turnaround time for all 381 reviews was 3.5 business days. • The adult donor selections and prioritization from the HLA Search Strategy Advisors were compared to the prioritization of the HapLogic software for 118 searches (statistical sample volume). The comparisons occurred in October/November 2006, the summary was prepared in April – pending revisions should be complete in May 2007.
II.B. Rapid Identification of Matched Donors – Hypothesis 4: Reducing the time and effort required to identify closely matched donors for patients in urgent need of HSC transplants will improve access to transplantation and patient survival in the context of a contingency response and routine patient care.	
Aim B.4.1: Expand Network Communica-tions	**Period 6 Activity:** • For STAR II, work performed has been to support the Electronic Workup effort. STAR II will be using web services to help reduce layers in the communication process as well as putting NMDP on a path to a more secure, standardized transaction system. STAR II has additionally made maintenance changes to support HML, IDML, CORD Link and the Web Scripts. • As always, STAR II will serve as an insulating layer between software systems and will provide backwards compatibility as changes occur. Support for two way XML transactions will be released before the Electronic Workup project and will provide for greater flexibility in the NMDP transaction system. • All NMDP HLA search strategy advisors completed 381 search reviews for 88 transplant centers in this quarter. External advisors completed 241 reviews with an average turnaround time of 4.4 business days; internal advisors provided 140 reviews with an average turnaround time of 2.6 business days. The average turnaround time for all 381 reviews was 3.5 business days.

Aim B.4.2: Central Contingency Management	**Period 6 Activity:** • In this quarter 54 total Custom Search Support reviews were completed by the internal HLA search advisors. For the two transplant centers with all patients enrolled, 52 Custom Search Support reviews were provided (36 and 16 reviews, respectively). Two additional centers submitting selected patients received 1 review each.
II.C. Immunuogenetic Studies – Hypothesis 1: HLA mismatches may differ in their impact on transplant outcome, therefore, it is important to identify and quantify the influence of specific HLA mismatches. In contingency situations it will not be possible to delay transplant until a perfectly matched donor can be found.	
Aim C.1.1: Donor Recipient Pair Project	**Period 6 Activity:** Sample Group 14 (SG14) data audit is ongoing, with completion expected early next quarter. Data Audit work continues on Sample Group 15 (SG15). • Discrepancy analysis along with B/C and DRB linkage analysis was completed this quarter. • Shipping of replacement samples will occur early next quarter. Sample testing for Sample Group 16 (SG16) is currently underway with a period of performance ending April 30, 2007. • SG16 consists of 500 Donor/Recipient transplant pairs selected by CIBMTR Statistical Center. • All samples are being typed at intermediate HLA-A, B and DRB1 and at high resolution HLA-A, B C DRB1/3/4/5 DQA1 and DQB1 when results are not available from the transplant center.
II.C. Immunuogenetic Studies – Hypothesis 2: Even when patient and donor are HLA matched, GVHD occurs so other loci may play a role.	
Aim C.2.1: Analysis of non-HLA loci	**Period 6 Activity:** • Typing began for Phase 3 of the High Resolution Killer Immunoglobulin-like Receptor (KIR) Typing Project. The period of performance is January 1, 2007-September 30, 2007 and contains 165 samples to be typed in duplicate at two laboratories at 14 loci. Phase 3 of the project consists of 165 Caucasian donor samples from T-cell replete transplants for Acute Myelogenous Leukemia and Chronic Myelogenous Leukemia. Laboratories continue to resolve discrepancies and ambiguities identified in Phase 1 and 2 of the project. At

	the completion of Phase 3, 435 samples will be typed at high resolution. • The Scientific Services and Information Systems departments continue to collaborate on the design and development of a new non-HLA database and database tools to support the KIR Pilot Project. Data from this project will be linked to high resolution HLA and clinical outcome data for analysis.
Aim C.2.2: Related Pairs Research Repository	**Period 6 Activity:** • HRSA approved the Related Repository implementation plan for the Stem Cell Therapeutics Outcome Database. • A meeting was held at the BMT Tandem Meeting with the medical directors of the seven selected pilot transplant centers to solicit feedback on the implementation plan. The plan was well received with only minor recommendations for changes including shipment of individual samples rather than pairs due to logistical issues and the preference for receipt of pre-printed sample labels to ease submission. • Modifications to the NMDP Repository protocol and consents were completed and submitted to the NMDP IRB for review and approval. IRB approval is expected early next quarter. • NMDP Scientific Services, Bioinformatics and IT staff began planning the Repository inventory software and database modifications to facilitate the receipt, processing, storage and retrieval of the related samples.
II.D. Clinical Research in Transplantation – Hypothesis 1: Clinical research in transplantation improves transplant outcomes and supports preparedness for a contingency response.	
Aim D.1.1: Observational Research, Clinical Trials and NIH Transplant Center	**Period 6 Activity:** • A total of 8 patients screened for enrollment in the Renal Cell Carcinoma (RCC) trial. Two did not meet criteria while 6 remain in process of screening. A total of 5 sites participating in trial. One site closed to enrollment due to low accrual. • Accrual and recruitment initiative planning occurred for the RCC trail during this period. Initiated monthly Investigator meetings in February. • Double Cord trial received NMDP IRB approval and protocol/consents released to all participating centers in January. Site IRB in progress. • Database design and development initiated and well underway during this reporting period.

	• Coordination of an Investigator meeting at the May Cord Blood Symposium planned. • Twenty-five donor/patient pairs enrolled and randomized on the PBSC vs. Marrow trial for a total of 249. • Staff continued to identify activities to increase accrual on the PVM trial. Two sessions were organized for presentation at the NMDP Spring Meeting. • The Clinical Trial Advisory Board of the CIBMTR met in February. One proposal was reviewed during the meeting but was denied. In addition, the Board's Charter was reviewed and revisions suggested. • Staff continued work on various observational studies. Final two training programs were held during this period. Review and prioritization of studies occurred during the Tandem meetings in February.
Aim D.1.2: Research with NMDP Donors	**Period 6 Activity:** Following is the activity that has taken place on the study examining the impact race and culture has on a donor's decision to proceed through the confirmatory testing and donation process. • A sub-award with the University of Pittsburgh has been signed; • The algorithm for donor selection is finalized; • Two staff members within NMDP Research Operations have been trained to make the initial donor calls to invite donors to learn more about the study; • Study will be open for enrollment in mid-April.
Aim D.1.3: Expand Immuno-biology Research	**Period 6 Activity:** The CIBMTR Immunobiology Working Committee (IBWC) held its annual meeting at the BMT Tandem Meetings on February 9 in Keystone, Colorado. • Over the past year there were 33 active studies and five studies published or submitted for publication. • Four new proposals were reviewed and three approved for implementation in the next academic year (July 2007-June 2008). One proposal was rejected for overlap with an existing study. • Study progress reports were presented by all principal investigators in attendance. • The committee membership was provided information on the availability of limited research funding for IBWC studies that support the NMDP's research priorities. Funding for CIBMTR Immunobiology Working Committee (IBWC) studies. • The DNA extraction laboratory successfully completed the optimization of the granulocyte protocol. The

	final extraction protocols were written into the scope of work and the contract finalized. The remaining 2500 samples will be shipped following execution of the contract early next quarter. • A funding request to provide support for technical staff and reagent support for a study investigating the role of chemokine and chemokine receptor polymorphisms in graft versus host disease was approved by the IBWC leadership. The award notification and contract were prepared and sent to the requestor. Final execution and award disbursement is expected early next quarter.

National Marrow
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April 27, 2007

Commander Russell Shilling, USN
Program Officer, Medical Services Corps
Office of Naval Research (ONR 341)
875 N. Randolph St.
Arlington, VA 22203

Subject: Quarterly Performance/Technical Report of the National Marrow Donor Program®

Reference: Grant Award #N00014-06-1-0704 between the Office of Naval Research and the National Marrow Donor Program

Dear Commander Shilling:

Enclosed is subject document which provides the performance activity for each statement of work task item of the above reference for the period of January 1, 2007 to March 31, 2007.

Should you have any questions as to the scientific content of the tasks and the performance activity of this progress report, you may contact our Chief Operating Officer - Patricia Coppo directly at 612-627-5815.

With this submittal of the quarterly progress report, the National Marrow Donor Program has satisfied the reporting requirements of the above reference for quarterly documentation.

Please direct any questions pertaining to the cooperative agreement to my attention (612-362-3403 or at cabler@nmdp.org).

Sincerely,

Carla Abler-Erickson

Carla Abler-Erickson, MA
Sr. Contracts Representative

Enclosure: One (1) copy of SF298

c: R. Baerga – ACO (ONR-Chicago), letter and enclosure
Dr. Robert J. Hartzman, CAPT, MC, USN (Ret): letter and enclosure
DTIC (Ste 0944): letter and enclosure
NRL (Code 5227): letter and enclosure
Brian Bradley – Grants Officer (ONR-252), letter and enclosure
Patricia A. Coppo, Chief Operating Officer, NMDP, letter

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14. ABSTRACT

1. Contingency Prepardness: Collect information from transplant centers, build awareness of the Transplant Center Contingency Planning Committee and educate the transplant community about the critical importance of establishing a nationwide contingency response plan.

2. Rapid Identification of Matched Donors : Increase operational efficiencies that accelerate the search process and increase patient access are key to preparedness in a contingency event.

3. Immunogenetic Studies: Increase understanding of the immunologic factors important in HSC transplantation.

4. Clinical Research in Transplantation: Create a platform that facilitates multicenter collaboration and data management.

15. SUBJECT TERMS
Research in HLA Typing, Hematopoietic Stem Cell Transplantation and Clinical Studies to Improve Outcomes

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U	U	U			19b. TELEPONE NUMBER *(Include area code)* (612) 627-5850

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QUARTERLY
PERFORMANCE / TECHNICAL REPORT
FOR
JANUARY 1, 2007 to MARCH 31, 2007

Office of Naval Research

And

The National Marrow Donor Program
3001 Broadway Street N.E.
Minneapolis, MN 55413
1-800-526-7809

QUARTER PROGRESS REPORT

Development of Medical Technology for Contingency Response to Marrow Toxic Agents

January 01, 2007 through March 31, 2007

TABLE OF CONTENTS

ACRONYM LIST

AABB – American Association of Blood Banks
AML – Acute Myelogenous Leukemia
ARS – Acute Radiation Syndrome (also known as Acute Radiation Sickness)
ASBMT – American Society for Blood and Marrow Transplantation
ASHI – American Society for Histocompatability and Immunogenetics
B-LCLs – B-Lymphoblastoid Cell Lines
BMT-CTN – Blood and Marrow Transplant - Clinical Trials Network
C&A – Certification and Accreditation
CBMTG – Canadian Blood and Marrow Transplant Group
CBB – Cord Blood Bank
CBC – Congressional Black Caucus
CBS – Canadian Blood Service
CBU – Cord Blood Unit
CHTC – Certified Hematopoeitic Transplant Coordinator
CIBMTR – Center for International Blood & Marrow Transplant Research
CLIA – Clinical Laboratory Improvement Amendment
CME – Continuing Medical Education
CREG – Cross Reactive Groups
CT – Confirmatory Typing
CTA – Clinical Trial Application
DIY – Do it yourself
DKMS – Deutsche Knochenmarkspenderdatei
DMSO - Dimethylsulphoxide
DNA – Deoxyribonucleic Acid
D/R – Donor/Recipient
EBMT – European Group for Blood and Marrow Transplantation
EM – Expectation Maximization
EMDIS – European Marrow Donor Information System
FBI – Federal Bureau of Investigation

FDA – Food and Drug Administration
Fst – Fixation Index
GETS – Government Emergency Telecommunications Service
GCSF – Granulocyte-Colony Stimulating Factor (also known as filgrastim)
GVHD – Graft vs Host Disease
HHS – Health and Human Services
HIPAA – Health Insurance Portability and Accountability Act
HLA – Human leukocyte antigen
HMD – Histoimmunogenetics Mark-up Language
HML – *Histoimmunogenetics* Mark-up Language
HR – High Resolution
HRSA – Health Resources and Services Administration
HSC – Hematopoietic stem cell
IBWC – Immunobiology Working Committee
IDM – Infectious disease markers
IHWG – International Histocompatibility Working Group
IND – Investigational New Drug
ICRHER – International Consortium for Research on Health Effects of Radiation
IS – Information services
IT – Information technology
IRB – Institutional Review Board
IHWG – International Histocompatibility Working Group
KIR – Killer Immunoglobulin-like Receptor
NCI – National Cancer Institute
MHC – Major Histocompatibility Complex
MICA – MHC Class I-Like Molecule, Chain A
MICB – MHC Class I-Like Molecule, Chain B
MUD – Matched Unrelated Donor
NCBM – National Conference of Black Mayors
NCI – National Cancer Institute
NHLBI – National Heart, Lung and Blood Institute

NIAID – National Institute for Allergy and Infectious Disease
NIH – National Institutes of Health
NIMS – National Incident Management System
NK – Natural Killers
NMDP – National Marrow Donor Program
NRP – National Response Plan
NST – Non-myeloablative Allogeneic Stem Cell Transplantation
OCR/ICR – Optical Character Recognition/Intelligent Character Recognition
OIT – Office of Information Technology
OMB – Office of Management and Budget
ONR – Office of Naval Research
PBMCs – Peripheral Blood Mononuclear Cells
PBSC – Peripheral Blood Stem Cell
PCR – Polymerase Chain Reaction
P-LCLs – B-lymphoblastoid cell lines
PSA – Public Service Announcement
QC – Quality control
RCC – Renal Cell Carcinoma
REAC/TS – Radiation Emergency Assistance Center/Training Site
RFP – Request for Proposal
RFQ – Request for Quotation
RITN – Radiation Injury Transplant Network
SBT – Sequence Based Testing
SCTOD – Stem Cell Therapeutics Outcome Database
SG – Sample Group
SSP – Sequence Based Priming
SSOP – Sequence Specific Oligonucleotide Probes
STAR® – Search, Tracking and Registry
TC – Transplant Center
TED – Transplant Essential Data
TNC – Total Nucleated Cell

TSA – Transportation Security Agency
URD – Unrelated Donor
WMDA – World Marrow Donor Association
WU – Work-up

IIA. Contingency Preparedness – Hypothesis 1: Recovery of casualties with significant myelosuppression following radiation or chemical exposure is optimal when care plans are designed and implemented by transplant physicians	
IIA.1.1 Aim 1: Secure Interest of Transplant Physicians	**Period 2 Activity:** **<u>Funding provided by both 0859 and 0704 contracts this quarter:</u>** • Initiated planning of physician radiological/nuclear emergency training seminar: o Scheduled for September 25, 2007 in Bethesda, MD. o Seminar title: Medical and organizational challenges resulting from a radiological or nuclear emergency. o Anticipating 150 attendees. o Seminar objective: Inform attendees of the biological risk factors and medical complications resulting from ionizing radiation exposure and to diagnose various resulting injuries. o Program description: Presentations of the impact to the US and the medical challenges that would arise due to an ionizing radiation event o Learning objectives: ▪ Understand the current radiation/nuclear threat to the US. ▪ Describe biological effects of ionizing radiation on the multiple organs (skin, hematological, GI, neurological, and multi-organ failure). ▪ Explain basics of calculating radiation dose based on bio-dosimetry. ▪ Describe current concept of operations from triage through delivery of care or transfer to another treatment facility. ▪ Hospital management of severely injured radiation patients. • Began the development of a standardized RITN ARS Grand Rounds presentation for use by all RITN centers.
IIA.1.2 Aim 2: GCSF in Radiation Exposure	**Period 2 Activity:** • No activity this period.

IIA.1 3 Aim 3: Patient Assessment Guidelines	**Period 2 Activity:** • No activity this period.
IIA 1.4 Aim 4: National Data Collection Model	**Period 2 Activity:** • No activity this period.
IIA. Contingency Preparedness – Hypothesis 2: Coordination of the care of casualties who will require hematopoietic support will be essential in a contingency situation.	
IIA.2.1 Aim 1: Contingency Response Network	**Period 2 Activity:** **Funding provided by both 0859 and 0704 contracts this quarter:** **Planning:** • Developed a RITN Web site outside the NMDP Network site (www.nmdp.org/ritn) • Created and distributed RITN SOP templates for TCs, DCs, and CBBs. • Coordinated approval for release of sanitized TC SOP as an example for other RITN centers. • Produced and distributed a contact list with RITN points of contact, key federal agencies and state emergency operation center contacts. • Created organization level Emergency Response Plan, and coordinated training of all staff during 3rd quarter. **Exercises:** • Participated in a regional tabletop exercise focusing on the detonation of an Improvised Nuclear Device (IND) held by the MN Federal Executive Board. **Meetings:** • Presented a RITN overview presentation to HHS-NCI parallel preparedness initiative. • Held a RITN meeting at the ASBMT/CIBMTR Tandem Meetings in February. • Continued to coordinate signing of RITN agreements; as of April 11, 2007, 73% (44 of 60) of invited centers have signed participation agreements. • Attended the NIAID Radiation Combined Injury Workshop in Bethesda, MD.

	• Assisted multiple RITN centers in developing their response plans (support provided via conference call). • Performed a site visit at Barnes Jewish to consult on their development of RITN SOPs. **Communications:** • Purchased and distributed additional satellite telephones; a total of 36 phones are distributed to RITN centers. • Distributed additional GETS cards; there are a total of 114 cards between NMDP staff and RITN centers. • Conducted communication tests with the Network (January and March) and a GETS card user test.
IIA.2.2 Aim 2: Sibling Typing Standard Operating Procedures	**Period 2 Activity:** • It was determined this quarter that efforts toward this AIM will be to develop written SOPs that are independent of the existing NMDP Information Technology Systems. • These efforts will begin in FY 2008.
IIA. Contingency Preparedness – Hypothesis 3: NMDP's critical information technology infrastructure must remain operational during contingency situations that directly affect the Coordinating Center.	
IIA.3.1 Aim 1: I.S. Disaster Recovery	**Period 6 Activity:** • No activity this period.
IIB. Rapid Identification of Matched Donors – Hypothesis 1: Increasing the resolution and quality of the HLA testing of volunteers on the registry will speed donor selection.	
IIB.1.1 Aim 1: Increase Registry Diversity	**Period 2 Activity:** • No activity this period.
IIB.1.2 Aim 2: Evaluate HLA-DRB1 High Res typing	**Period 2 Activity:** • No activity, this task is closed.

IIB.1.3 Aim 3: Evaluate HLA-C Typing of Donors	**Period 2 Activity:** • No activity, this task is closed.
IIB.1.4 Aim 4: Evaluate Buccal Swabs	**Period 2 Activity:** • No Activity this period.
IIB 1.5 Aim 5: Enhancing HLA Data for Selected Donors	**Period 2 Activity:** Development of a project plan for the Replacement Donor Pilot Project began January of 2007. • Required system elements and reports were identified and developed, and a comprehensive interdepartmental project plan was developed. • NMDP staff was trained and project plan tested in preparation for a March 1 start date. • A single high resolution HLA typing laboratory was secured for this project. • Donor Centers were given the option of either allowing the NMDP Call Back Unit to perform donor contacts or to participate directly in the project and contact their donors and collect needed study information. Conference call training for the centers selecting the later option was developed and conducted in mid-March. These donor centers will be phased into the project on April 1, 2007. The pilot study was initiated on schedule, beginning on March 1, 2007. • Patient searches with active work-up requests were reviewed by Scientific Services staff. • For those work-up requests where there is not one or more equivalently HLA matched potential replacement donors available, up to 5 potentially matched donors were selected (when available) for potential prospective high resolution HLA-A, -B, -C and -DRB1 typing. • Donor contacts were made to confirm availability, to provide education, to conduct an abbreviated medical history assessment and to send out a buccal swab kit if a repository sample was not available. • Over 350 searches were reviewed in the first month, with approximately 75 potential replacement donors selected for contact and potential prospective HLA typing. Further project statistics will be provided next quarter. Model building began in January for the "Optimal Donor Project" which is funded under this aim to selectively HLA type donors such that a fully high-resolution typed donor with optimal non-HLA characteristics appears for

	as many patient searching phenotypes as possible. The modeling is based on an analysis of the phenotype frequencies in the US and the status of matchlists for phenotypes above a frequency threshold.
IIB. Rapid Identification of Matched Donors – Hypothesis 2: Primary DNA typing data can be used within the registry to improve the quality and resolution of volunteer donor HLA assignments.	
IIB 2.1 Aim 1: Collection of Primary Data	**Period 2 Activity:** • Development of the HML electronic reporting format has continued during this period (version 0.4) to include a more generalized format for reporting single and multi-locus typings and group-specific-sequencing primers for sequencing-based-typings.
IIB 2.2 Aim 2: Validation of Logic of Primary Data	**Period 2 Activity:** • No activity, this task is closed.
IIB 2.3 Aim 3: Reinterpretation of Primary Data	**Period 2 Activity:** • No activity, this task is closed.
IIB 2.4 Aim 4: Genotype Lists & Matching Algorithm	**Period 2 Activity:** • During the previous period a comprehensive validation and loading of DRB1 SSO interpretation results has been implemented for all results that fall within 2-digit HLA DNA groups. Work is underway to smoothly integrate results into the matching algorithm where the re-interpretation includes alleles that span multiple 2-digit groups.
IIB. Rapid Identification of Matched Donors – Hypothesis 3: Registry data on HLA allele and haplotype frequencies and on the nuances of HLA typing can be used to design computer algorithms to predict the best matched donor.	
IIB.3.1 Aim 1: Phase I of EM Haplotype Logic	**Period 2 Activity:** • The design of the second phase of the HapLogic matching algorithm has been completed. This includes predictions of allele-match at HLA-C and HLA-DQB1. • Retrospective typing datasets have been selected for validation such that donors involved in the haplotype frequency estimation are not included in the validation.

IIB 3.2 Aim 2: Enhancement of EM Algorithm	**Period 2 Activity:** • A manuscript entitled "High resolution HLA alleles and haplotypes in the US population" was accepted for publication in the journal Human Immunology. This is the largest high-resolution typed HLA allele and haplotype frequency dataset ever published and all US minority donors are selected at random from the donor pool. • A follow-on manuscript describing the EM algorithm implementation is under development, which will include a description of the software NMDP has developed under this aim and access to that software.
IIB 3.3 Aim 3: Optimal Registry Size Analysis	**Period 2 Activity:** • A manuscript entitled "Estimation of HLA-A,B,DRB1 haplotype frequencies utilizing mixed resolution data from a national registry in the presence of selective retyping of volunteers" has been updated for a second submission to the journal Human Immunology. This manuscript is the technical foundation of NMDP registry size analyses. • A review committee of experts in the field of population genetics is being assembled to participate in an in-person meeting to review the approach NMDP has used for registry size analyses.
IIB 3.4 Aim 4: Target Under-represented Phenotypes	**Period 2 Activity:** • A set of prospective recruitment drives are being planned based on data generated under this aim to target donor recruitment to geographical regions where it is most likely to add the most new diversity to the registry. The target ZIP codes are being selected and refined based on the location existing recruitment resources.
IIB 3.5 Aim 5: Bioinformatics Web Site	**Period 2 Activity:** • High-resolution HLA allele frequencies have been published on this web site to accompany the manuscript in Human Immunology. This site contains the largest high-resolution HLA typed dataset where the donors were typed based on prospective typing projects (randomly selected from the donor pool).
IIB 3.6 Aim 6: Consultants to Improve Algorithm	**Period 2 Activity:** • A new version of the multiple-cord application has been released which includes a number of new features based on initial feedback from users. This application has been developed under this aim as an extension of tools used by consultants that has now been released to over 30 US transplant centers and is a

	working prototype of a global single/multiple cord blood unit selection tool.
IIB. Rapid Identification of Matched Donors – Hypothesis 4: Reducing the time and effort required to identify closely matched donors for patients in urgent need of HSC transplants will improve access to transplantation and patient survival in the context of a contingency response and routine patient care.	
IIB.4.1 Aim 1: Expand Network Communica-tions	**Period 2 Activity:** • No activity this period
IIB.4.2 Aim 2: Central Contingency Management	**Period 2 Activity:** • NMDP is currently providing Customized Search Support Services to three transplant centers that need to outsource donor selection and management activities for a variety of reasons, including a staff sabbatical. A physician focus group was held at the Tandem Meetings in Keystone to educate physicians about the service and receive feedback about any suggestions to enhance the service. NMDP is planning site visits during period 3 to three additional centers who have indicated interest.
IIC. Immunogenetic Studies – Hypothesis 1: HLA mismatches may differ in their impact on transplant outcome, therefore, it is important to identify and quantify the influence of specific HLA mismatches. In contingency situations it will not be possible to delay transplant until a perfectly matched donor can be found.	
IIC.1.1 Aim 1: Donor Recipient Pair Project	**Period 2 Activity:** • No activity this period.
IIC. Immunogenetic Studies – Hypothesis 2: Even when patient and donor are HLA matched, GVHD occurs so other loci may play a role.	
IIC 2.1 Aim 1: Analysis of non-HLA loci	**Period 2 Activity:** • Database development has ramped up on the development of the IPR (Immunobiology Project Results) database to store the results of the KIR typing project for analysis. • Haplotype analysis has been performed on the first two phases of the KIR typing project and will be included in a manuscript, under preparation, describing this project.

IIC 2.2 Aim 2: Related Pairs Research Repository	**Period 2 Activity:** • The first application in a suite of tools for managing data for the research repository has been released under this aim. These tools include laboratory contact management, sample selection, shipment request and scheduling.
IID. Clinical Research in Transplantation – Hypothesis 1: Clinical research in transplantation improves transplant outcomes and supports preparedness for a contingency response.	
IID.1.1 Aim 1: Observational Research, Clinical Trials and NIH Transplant Center	**Period 2 Activity:** • The NIH transplant center has one patient search at the formal search stage and one patient search at the workup stage with plans to transplant under the protocol for immunodeficiencies.
IID.1.2 Aim 2: Research with NMDP Donors	**Period 2 Activity:** • No activity this period.
IID.1.3 Aim 3: Expand Immuno-biology Research	**Period 2 Activity:** • No Activity this period.